

Final Report

August, 1996

NASA Interchange NCA2- 687

Immunological and Hematopoietic Biotechnology Studies

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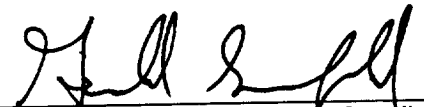
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INTRODUCTION

The purpose of the work carried under this interchanges was to support the development of space flight biotechnology experiments in the areas of immunology and hematopoiesis to facilitate the commercial development of space. The studies involved the interaction and development of experiments with biotechnology companies for necessary ground-based studies to allow the development of flight studies.

The thrust of the work was to develop experiments with the Chiron Corporation and Bioserve involving the use of interleukin-2 to modulate the effects of spaceflight on immune responses. Spaceflight has been shown to have multiple effects on immune responses (1). Interleukin-2 is an immunoregulator that could have potential to counter some of the alterations induced in immune responses by spaceflight (1).

To test this possibility before flight, rats were suspended antiorthostatically (2) and treated with interleukin-2. Antiorthostatic suspension is a model for some of the effects of spaceflight on immune responses (2). The interleukin-2 was given to see if it could alter some of the effects of suspension. This was achieved. As a result of these studies, two flight experiments were developed and flown with the Chiron Corp. And Bioserve to determine if use of interleukin-2 could prevent or attenuate the effects of space flight on immune responses.

METHODS

Rats were antiorthostatically suspended by the tail (2). At the commencement of suspension, some of the rats were treated with various doses of interleukin-2, a product of the Chiron Corporation, and control rats were treated with placebo. Other control rats were maintained in normal vivarium housing. At the end of the suspension period, immunological parameters of the rats were examined. These experiments were carried out more than 3 times.

Two sets of immunological parameters were examined. The first was the ability of interleukin-2 to prevent the loss of the ability of bone marrow cells from suspended to respond to granulocyte-macrophage colony stimulating factor (3). After suspension, femurs were removed from the rats and bone marrow was obtained. The bone marrow was placed in a semi-solid medium in tissue culture dishes. The medium also contained granulocyte-macrophage colony stimulating factors. Normally, the colony stimulating factor would cause colonies to form after at least one week of incubation, and suspension, as space flight, would inhibit this (3). After the incubation period, the number of colonies was determined microscopically.

The second parameter was interferon production, which has been shown to be altered by space flight and suspension (4). Spleens were removed from the rats after suspension and passed through screens to allow development of single cells cultures. The cultures were challenged with interferon inducers, and allowed to remain in culture for interferon-alpha/beta and interferon-gamma production. The culture supernatant fluids were then analyzed for interferon levels (4).

Additional experiments were attempted to determine leukocyte subset distribution by flow cytometry (3). These results did not appear to be reliable, and the experiments were dropped from actual flight studies.

RESULTS AND DISCUSSION

The results of this study indicated that treatment of rats with interleukin-2 reduced the inhibitory effects of suspension on the ability of bone marrow cells to respond to granulocyte-macrophage colony stimulating factor. Additionally, a trend to improvement of the interferon response was also observed. No useful data on flow cytometry were observed. In view of the results of these studies, two space flight experiments using interleukin-2 were designed and carried out with the Chiron Corp. And Bioserve.

PUBLICATIONS

A manuscript is currently in preparation. It will be forwarded when available.

REFERENCES

1. Taylor, G.R. Overview of spaceflight immunology studies. *J. Leukocyte Biology*, 54:179, 1993.
2. Chapes, S.K. Mastor, A.M., Sonnenfeld, G., and Berry, W.D. Antiorthostatic suspension as a model for the effects of spaceflight on the immune system. *J. Leukocyte Biology*. 54:227, 1993.
3. Sonnenfeld, G., Mandel, A.D., Konstantinova, I.V., Berry, W.D., Taylor, G.R., Lesnyak, A.T., Fuchs, B.B., Rakhmilevich, A.L. Spaceflight alters immune cell function and distribution. *J. Appl. Physiol.* 73:191S, 1992.
4. Gould, C.L., Lyte, M., Williams, J.A., Mandel, A.D., and Sonnenfeld, G. Inhibited interferon-gamma production but normal interleukin-2 production from rats flown on the space shuttle. *Aviat.*

Space Environ. Med. 58:983, 1987.